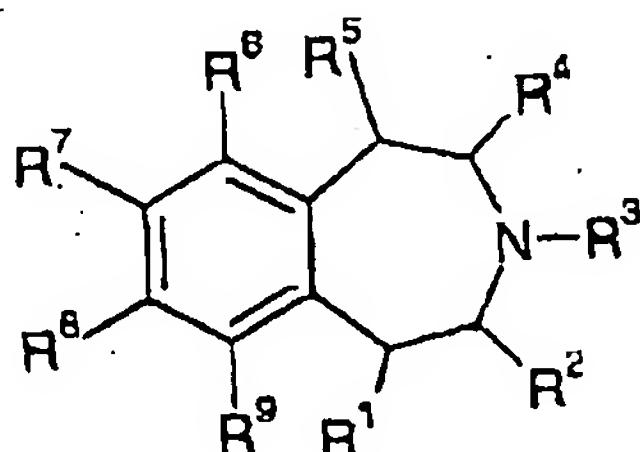


X-16115

-575-

WE CLAIM:

1. A compound of Formula I:



I

5 where:

R^1 is hydrogen, fluoro, or (C_1-C_3) alkyl;

R^2 , R^3 , and R^4 are each independently hydrogen, methyl, or ethyl;

R^5 is hydrogen, fluoro, methyl, or ethyl;

R^6 is $-C\equiv C-R^{10}$, $-O-R^{12}$, $-S-R^{14}$, or $-NR^{24}R^{25}$;

- 10 R^7 is hydrogen, halo, cyano, (C_1-C_6) alkyl optionally substituted with 1 to 6 fluoro substituents, (C_2-C_6) alkenyl optionally substituted with 1 to 6 fluoro substituents, (C_3-C_7) cycloalkyl, (C_1-C_6) alkoxy optionally substituted with 1 to 6 fluoro substituents, (C_1-C_6) alkylthio optionally substituted with 1 to 6 fluoro substituents, $Ph^1-(C_0-C_3)$ alkyl, $Ph^1-(C_0-C_3)$ alkyl-O-, or $Ph^1-(C_0-C_3)$ alkyl-S-;

15 R^8 is hydrogen, halo, cyano, or $-SCF_3$;

R^9 is hydrogen;

R^{10} is $-CF_3$, ethyl substituted with 1 to 5 fluoro substituents, (C_3-C_6) alkyl optionally substituted with 1 to 6 fluoro substituents, (C_3-C_7) cycloalkyl, (C_0-C_3) alkyl,

- 20 $Ar^1-(C_0-C_3)$ alkyl, $Ph^1-(C_0-C_3)$ alkyl, or 3- (C_1-C_4) alkyl-2-oxo-imidazolidin-1-yl- (C_1-C_3) alkyl;

R^{12} is $Ph^2-(C_1-C_3)$ alkyl, $Ar^2-(C_1-C_3)$ alkyl, (C_1-C_6) alkyl-S- (C_2-C_6) alkyl, (C_3-C_7) cycloalkyl-S- (C_2-C_6) alkyl, phenyl-S- (C_2-C_6) alkyl, $Ph^2-S-(C_2-C_6)$ alkyl, phenylcarbonyl- (C_1-C_3) alkyl, $Ph^2-C(O)-(C_1-C_3)$ alkyl,

- 25 (C_1-C_6) alkoxycarbonyl- (C_3-C_6) alkyl, (C_3-C_7) cycloalkyl-OC(O)- (C_3-C_6) alkyl,

X-16115

-576-

phenyloxycarbonyl-(C₃-C₆)alkyl, Ph²-OC(O)-(C₃-C₆)alkyl, Ar²-OC(O)-(C₃-C₆)alkyl,
 (C₃-C₇)cycloalkyl-NH-C(O)-(C₂-C₄)alkyl-, Ph¹-NH-C(O)-(C₂-C₄)alkyl-,
 Ar²-NH-C(O)-(C₂-C₄)alkyl-, or R¹³-C(O)NH-(C₂-C₄)alkyl;

5 R¹³ is (C₃-C₇)cycloalkyl(C₀-C₃)alkyl, Ph¹, Ar², or (C₁-C₃)alkoxy optionally substituted
 with 1 to 6 fluoro substituents, Ph¹-NH- or N-linked Her¹;

R¹⁴ is Ar² which is not N-linked to the sulfur atom, Ph², R¹⁵-L-, tetrahydrofuranyl,
 tetrahydropyranyl, or phenyl-methyl substituted on the methyl moiety with a
 substituent selected from the group consisting of (C₁-C₃)-n-alkyl substituted with
 hydroxy, (C₁-C₃)alkyl-O-(C₁-C₂)-n-alkyl, (C₁-C₃)alkyl-C(O)-(C₀-C₂)-n-alkyl, and
 10 (C₁-C₃)alkyl-O-C(O)-(C₀-C₂)-n-alkyl,

wherein when R¹⁴ is Ph² or Ar², wherein Ar² is pyridyl, then R¹⁴ may also,

optionally be substituted with phenyl-CH=CH- or phenyl-C≡C-,

said phenyl-CH=CH- or phenyl-C≡C- being optionally further

substituted with 1 to 3 substituents independently selected from the

15

group consisting of halo, cyano, -SCF₃, (C₁-C₆)alkyl optionally

further substituted with 1 to 6 fluoro substituents, and

(C₁-C₆)alkoxy optionally further substituted with 1 to 6 fluoro
 substituents, and

wherein when Ar² is pyridyl, the pyridyl may alternatively, optionally be

20

substituted with R²⁸R²⁹N-C(O)-, and optionally further substituted with

one methyl, -CF₃, cyano, or -SCF₃ substituent, or with 1 to 2 halo

substituents, and

wherein the tetrahydrofuranyl and tetrahydropyranyl may optionally be

substituted with an oxo substituent, or with one or two groups

25

independently selected from methyl and -CF₃;

R¹⁵ is -OR¹⁶, cyano, -SCF₃, Ph², Ar², quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl,
 phthalimido, benzothiophenyl optionally substituted at the 2-position with phenyl or
 benzyl, benzothiazolyl optionally substituted at the 2-position with phenyl or benzyl,
 benzothiadiazolyl optionally substituted with phenyl or benzyl, 2-oxo-dihydroindol-1-
 30 yl optionally substituted at the 3 position with gem dimethyl or (C₁-C₆)alkyl
 optionally further substituted with 1 to 6 fluoro substituents, 2-oxo-dihydroindol-5-yl

X-16115

-577-

optionally substituted at the 3 position with gem dimethyl or (C₁-C₆)alkyl optionally further substituted with 1 to 6 fluoro substituents, 2-oxo-imidazolidin-1-yl optionally substituted at the 3 position with gem dimethyl or (C₁-C₆)alkyl optionally further substituted with 1 to 6 fluoro substituents, 2-oxo-tetrahydropyrimidinyl optionally substituted at the 3 or 4 position with gem dimethyl or (C₁-C₆)alkyl optionally further substituted with 1 to 6 fluoro substituents, 2-oxo-tetrahydroquinolin-1-yl optionally substituted at the 3 position with gem dimethyl or (C₁-C₆)alkyl optionally further substituted with 1 to 6 fluoro substituents, 2-oxo-dihydrobenzimidazol-1-yl optionally substituted at the 3 position with gem dimethyl or (C₁-C₆)alkyl optionally further substituted with 1 to 6 fluoro substituents, -NR¹⁷R¹⁸, -C(O)R²², or a saturated heterocycle selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, and thiomorpholinyl, tetrahydrofuranyl, and tetrahydropyranyl,

wherein Ph² and Ar² when Ar² is pyridyl, may also optionally be substituted

with phenyl-CH=CH- or phenyl-C≡C-,

said phenyl-CH=CH- and phenyl-C≡C- being optionally further

substituted on the phenyl moiety with 1 to 3 substituents

independently selected from the group consisting of halo, cyano,

-SCF₃, (C₁-C₆)alkyl optionally further substituted with 1 to 6 fluoro substituents, and (C₁-C₆)alkoxy optionally further substituted with

1 to 6 fluoro substituents, and

wherein Ar² may alternatively, optionally be substituted with a substituent

selected from the group consisting of (C₃-C₇)cycloalkyl-(C₀-C₃)alkyl,

Het¹-(C₀-C₃)alkyl, pyridyl-(C₀-C₃)alkyl, and phenyl-(C₀-C₃)alkyl, and

optionally further substituted with one methyl, -CF₃, cyano, or -SCF₃

substituent, or with 1 to 2 halo substituents,

said pyridyl-(C₀-C₃)alkyl and phenyl-(C₀-C₃)alkyl optionally being

further substituted with 1-3 substituents independently selected

from halo, -CH₃, -OCH₃, -CF₃, -OCF₃, -CN, and -SCF₃, and

wherein when Ar² is pyridyl, the pyridyl may alternatively, optionally be

substituted with R²⁸R²⁹N-C(O)-, or (C₁-C₆)alkyl-C(O)- optionally

substituted with 1 to 6 fluoro substituents, and may be optionally further

X-16115

-578-

substituted with one methyl, -CF₃, cyano, or -SCF₃ substituent, or with 1 to 2 halo substituents, and

wherein when Ar² is thiazolyl, the thiazolyl may alternatively, optionally be substituted with (C₃-C₇)cycloalkyl-(C₀-C₃)alkyl-NH-, and

5 wherein the pyrrolidinyl, piperidinyl, morpholinyl, and thiomorpholinyl is substituted with oxo- on a carbon atom adjacent to the ring nitrogen atom, or is N-substituted with a substituent selected from the group consisting of

10 (C₁-C₆)alkylcarbonyl, (C₁-C₆)alkylsulfonyl,
(C₃-C₇)cycloalkyl(C₀-C₃)alkyl-C(O)-,
(C₃-C₇)cycloalkyl(C₀-C₃)alkyl-S(O)₂-, Ph¹-(C₀-C₃)alkyl-C(O)-, and
Ph¹-(C₀-C₃)alkyl-S(O)₂-, and

may optionally be further substituted with 1 or 2 methyl or -CF₃ substituents, and when oxo-substituted, may optionally be further N-substituted with a substituent selected from the group consisting of
15 (C₁-C₆)alkyl optionally further substituted with 1 to 6 fluoro substituents, (C₃-C₇)cycloalkyl(C₀-C₃)alkyl, and Ph¹-(C₀-C₃)alkyl, and

wherein tetrahydrofuranyl and tetrahydropyranyl may optionally be substituted with an oxo substituent, and/or with one or two groups
20 independently selected from methyl and -CF₃;

L is branched or unbranched (C₁-C₆)alkylene, except when R¹⁵ is -NR¹⁷R¹⁸ or

Ar²-N-linked to L, in which case L is branched or unbranched (C₂-C₆)alkylene, and when L is methylene or ethylene, L may optionally be substituted with gem-ethano or with 1 to 2 fluoro substituents, and when R¹⁵ is Ph², Ar², or a saturated heterocycle, L
25 may alternatively, optionally be substituted with a substituent selected from the group consisting of hydroxy, cyano, -SCF₃, (C₁-C₆)alkoxy optionally further substituted with 1 to 6 fluoro substituents, (C₁-C₆)alkoxycarbonyl optionally further substituted with 1 to 6 fluoro substituents, (C₁-C₆)alkylcarbonyloxy optionally further substituted with 1 to 6 fluoro substituents, (C₃-C₇)cycloalkyl-(C₀-C₃)alkyl-O-,
30 (C₃-C₇)cycloalkyl-(C₀-C₃)alkyl-O-C(O)-, and (C₃-C₇)cycloalkyl-(C₀-C₃)alkyl-C(O)-O-;

X-16115

-579-

- R^{16} is hydrogen, (C_1-C_6) alkyl optionally substituted with 1 to 6 fluoro substituents, (C_1-C_6) alkylcarbonyl, (C_3-C_7) cycloalkyl (C_0-C_3) alkyl, (C_3-C_7) cycloalkyl (C_0-C_3) alkyl-C(O)-, $Ph^1-(C_0-C_3)$ alkyl, $Ph^1-(C_0-C_3)$ alkyl-C(O)-, $Ar^2-(C_0-C_3)$ alkyl, or $Ar^2-(C_0-C_3)$ alkyl-C(O)-,
- 5 R^{17} is (C_1-C_4) alkyl optionally substituted with 1 to 6 fluoro substituents, *i*-butylsulfonyl, (C_3-C_7) cycloalkyl (C_0-C_3) alkyl-C(O)-, (C_3-C_7) cycloalkyl (C_0-C_3) alkyl-sulfonyl, $Ph^1-(C_0-C_3)$ alkyl, $Ph^1-(C_0-C_3)$ alkyl-C(O)-, $Ph^1-(C_0-C_3)$ alkylsulfonyl, $Ar^2-(C_0-C_3)$ alkyl, $Ar^2-(C_0-C_3)$ alkyl-C(O)-, $Ar^2-(C_0-C_3)$ alkylsulfonyl, $R^{19}OC(O)-$, or $R^{20}R^{21}NC(O)-$;
- 10 R^{18} is hydrogen or (C_1-C_4) alkyl optionally substituted with 1 to 6 fluoro substituents, or R^{17} and R^{18} , taken together with the nitrogen atom to which they are attached form Het¹ where Het¹ is substituted with oxo- on a carbon atom adjacent to the ring nitrogen atom, or R^{17} and R^{18} , taken together with the nitrogen atom to which they are attached, form an
- 15 aromatic heterocycle selected from the group consisting of pyrrolyl, pyrazolyl, imidazolyl, 1,2,3-triazolyl, and 1,2,4-triazolyl, said aromatic heterocycle optionally being substituted with 1 to 2 halo substituents, or substituted with 1 to 2 (C_1-C_4) alkyl substituents optionally further substituted with 1 to 3 fluoro substituents, or mono-substituted with
- 20 fluoro, nitro, cyano, $-SCF_3$, or (C_1-C_4) alkoxy optionally further substituted with 1 to 3 fluoro substituents, and optionally further substituted with a (C_1-C_4) alkyl substituent optionally further substituted with 1 to 3 fluoro substituents;
- R^{19} is (C_1-C_6) alkyl optionally substituted with 1 to 6 fluoro substituents, (C_3-C_7) cycloalkyl (C_0-C_3) alkyl, $Ar^2-(C_0-C_3)$ alkyl, or $Ph^1-(C_0-C_3)$ alkyl,
- 25 R^{20} is (C_1-C_6) alkyl optionally substituted with 1 to 6 fluoro substituents, (C_3-C_7) cycloalkyl (C_0-C_3) alkyl, $Ar^2-(C_0-C_3)$ alkyl, or $Ph^1-(C_0-C_3)$ alkyl,
- R^{21} is hydrogen or (C_1-C_4) alkyl optionally substituted with 1 to 6 fluoro substituents, or R^{20} and R^{21} , taken together with the nitrogen atom to which they are attached, form
- 30 Het¹;

X-16115

-580-

R^{22} is (C_1-C_6) alkyl optionally substituted with 1 to 6 fluoro substituents,

(C_3-C_7) cycloalkyl (C_0-C_3) alkyl, $R^{23}-O-$, $Ph^1-(C_0-C_3)$ alkyl, $Ar^2-(C_0-C_3)$ alkyl, or $R^{32}R^{33}N-$;

R^{23} is (C_1-C_6) alkyl optionally substituted with 1 to 6 fluoro substituents,

5 (C_3-C_7) cycloalkyl (C_0-C_3) alkyl, $Ph^1-(C_0-C_3)$ alkyl, or $Ar^2-(C_0-C_3)$ alkyl;

R^{24} is (C_1-C_6) alkoxy (C_2-C_5) alkyl optionally substituted with 1 to 6 fluoro substituents,

(C_1-C_6) alkylthio (C_2-C_5) alkyl optionally substituted with 1 to 6 fluoro substituents,

(C_3-C_7) cycloalkyl (C_0-C_1) alkyl- $O-(C_1-C_5)$ alkyl,

(C_3-C_7) cycloalkyl (C_0-C_1) alkyl- $S-(C_1-C_5)$ alkyl, phenyl (C_1-C_3) *n*-alkyl,

10 $Ph^2-(C_1-C_3)-n$ -alkyl, $Ar^2(C_0-C_3)$ *n*-alkyl, phenyl (C_0-C_1) alkyl- $O-(C_1-C_5)$ alkyl,

phenyl (C_0-C_1) alkyl- $S-(C_1-C_5)$ alkyl, $Ph^1-(C_0-C_1)$ alkyl- $C(O)NH-(C_2-C_4)$ alkyl,

$Ph^1-(C_0-C_1)$ alkyl- $NH-C(O)NH-(C_2-C_4)$ alkyl,

pyridyl- (C_0-C_1) alkyl- $C(O)NH-(C_2-C_4)$ alkyl,

pyridyl- (C_0-C_1) alkyl- $NH-C(O)NH-(C_2-C_4)$ alkyl, or $Ar^3(C_1-C_2)$ alkyl,

15 where Ar^3 is a bi-cyclic moiety selected from a group consisting of indanyl, indolyl,

dihydrobenzofuranyl, benzofuranyl, benzothiophenyl, benzoxazolyl,

benzothiazolyl, benzo[1,3]dioxolyl, naphthyl, dihydrobenzopyranyl, quinolinyl,

isoquinolinyl, and benzo[1,2,3]thiadiazolyl,

said Ar^3 optionally being substituted with (C_1-C_6) alkyl optionally further

20 substituted with 1 to 6 fluoro substituents, phenyl (C_0-C_1) alkyl optionally

further substituted with 1 to 6 fluoro substituents, or substituted with

(C_3-C_7) cycloalkyl (C_0-C_3) alkyl, or substituted with 1-3 substituents

independently selected from the group consisting of halo, oxo, methyl, and

- CF_3 ,

25 said phenyl (C_1-C_3) *n*-alkyl, $Ph^2-(C_1-C_3)$ *n*-alkyl, or $Ar^2(C_0-C_3)$ *n*-alkyl

optionally being substituted on the *n*-alkyl moiety when present with

(C_1-C_3) alkyl, dimethyl, gem-ethano, 1 to 2 fluoro substituents, or $(C_1-$

$C_6)$ alkyl- $C(O)-$,

said $Ar^2(C_0-C_3)$ *n*-alkyl being alternatively optionally substituted with a

30 substituent selected from the group consisting of (C_3-C_7) cycloalkyl-

(C_0-C_3) alkyl, $Het^1-(C_0-C_3)$ alkyl, pyridyl- (C_0-C_3) alkyl, phenyl-

X-16115

-581-

(C₀-C₃)alkyl, pyridyl-(C₀-C₃)alkyl-NH-, phenyl-(C₀-C₃)alkyl-NH-,
(C₁-C₆)alkyl-S-, and (C₃-C₇)cycloalkyl-(C₀-C₃)alkyl-S-, and optionally
further substituted with one methyl, -CF₃, cyano, or -SCF₃ substituent, or
with 1 to 2 halo substituents,

5 said pyridyl-(C₀-C₃)alkyl and phenyl-(C₀-C₃)alkyl optionally being
further substituted with 1-3 substituents independently selected
from halo, -CH₃, -OCH₃, -CF₃, -OCF₃, -CN, and -SCF₃, and

said Ph²-(C₁-C₃) *n*-alkyl and Ar²(C₀-C₃) *n*-alkyl where Ar² is pyridyl, also
optionally being substituted on the phenyl or Ar² moiety, respectively,
with phenyl-CH=CH- or phenyl-C≡C-,

10 said phenyl-CH=CH- or phenyl-C≡C- being optionally further
substituted with 1 to 3 substituents independently selected from the
group consisting of halo, cyano, -SCF₃, (C₁-C₆)alkyl optionally
further substituted with 1 to 6 fluoro substituents, and
15 (C₁-C₆)alkoxy optionally further substituted with 1 to 6 fluoro
substituents, and

said Ar²(C₀-C₃) *n*-alkyl where Ar² is pyridyl, alternatively, optionally being
substituted with (C₁-C₆)alkyl-C(O)- or R²⁸R²⁹N-C(O)-, and optionally
further substituted with one methyl, -CF₃, cyano, or -SCF₃ substituent, or
with 1 to 2 halo substituents,

20 said phenyl(C₀-C₁)alkyl-O-(C₁-C₅)alkyl, or phenyl(C₀-C₁)alkyl-S-(C₁-C₅)alkyl
optionally being substituted on the phenyl moiety with (C₁-C₂)-S(O)₂-, or
with 1 to 5 independently selected halo substituents, or with 1 to 3
substituents independently selected from the group consisting of halo,
25 cyano, -SCF₃, (C₁-C₆)alkyl optionally further substituted with 1 to 6 fluoro
substituents, and (C₁-C₆)alkoxy optionally further substituted with 1 to 6
fluoro substituents, and

said pyridyl-(C₀-C₁)alkyl-C(O)NH-(C₂-C₄)alkyl and
pyridyl-(C₀-C₁)alkyl-NH-C(O)NH-(C₂-C₄)alkyl optionally being
substituted on the pyridyl moiety with methyl, -CF₃, or 1 to 3 halo
30 substituents;

X-16115

-582-

R^{25} is hydrogen, (C_1-C_3) alkyl optionally substituted with 1 to 6 fluoro substituents, or allyl;

R^{26} is hydrogen, (C_1-C_6) alkyl optionally substituted with 1 to 6 fluoro substituents, (C_3-C_7) cycloalkyl (C_0-C_3) alkyl;

5 R^{27} is hydrogen or (C_1-C_4) alkyl optionally substituted with 1 to 6 fluoro substituents, or R^{26} and R^{27} , taken together with the nitrogen atom to which they are attached, form Het^1 ;

R^{28} is (C_1-C_8) alkyl optionally substituted with 1 to 6 fluoro substituents,

10 (C_3-C_8) cycloalkyl (C_0-C_3) alkyl, tetrahydropyran-3-yl (C_0-C_3) alkyl, tetrahydropyran-4-yl (C_0-C_3) alkyl, tetrahydrofuranyl (C_0-C_3) alkyl, $Ph^1-(C_0-C_2)$ *n*-alkyl, or $Ar^2-(C_0-C_2)$ *n*-alkyl,

said $Ph^1-(C_0-C_2)$ *n*-alkyl and $Ar^2-(C_0-C_2)$ *n*-alkyl optionally being substituted on the alkyl moiety when present with (C_1-C_3) alkyl, dimethyl, or gem-ethano;

R^{29} is hydrogen or (C_1-C_3) alkyl;

15 R^{30} is hydrogen, (C_1-C_6) alkyl optionally substituted with 1 to 6 fluoro substituents, (C_3-C_7) cycloalkyl (C_0-C_3) alkyl, $Ph^1-(C_0-C_3)$ alkyl, or $Ar^2(C_0-C_3)$ alkyl,

R^{31} is hydrogen or (C_1-C_6) alkyl optionally substituted with 1 to 6 fluoro substituents, or R^{30} and R^{31} , taken together with the nitrogen atom to which they are attached, form Het^1 ,

20 said Het^1 also optionally being substituted with phenyl optionally further substituted with 1 to 3 halo substituents;

R^{32} and R^{33} are each independently hydrogen or (C_1-C_6) alkyl optionally substituted with 1 to 6 fluoro substituents, or R^{32} and R^{33} , taken together with the nitrogen atom to which they are attached, form Het^1 , or R^{32} is $Ph^1(C_0-C_1)$ alkyl provided that R^{33} is

25 hydrogen;

Ar^1 is an aromatic heterocycle substituent selected from the group consisting of furanyl, thiophenyl, thiazolyl, oxazolyl, isoxazolyl, pyridyl, and pyridazinyl, any of which may optionally be substituted with 1 to 3 substituents independently selected from the group consisting of halo, (C_1-C_3) alkyl, (C_1-C_3) alkoxy, $-CF_3$, $-O-CF_3$, nitro, cyano, and

30 trifluoromethylthio;

X-16115

-583-

Ar² is an aromatic heterocycle substituent selected from the group consisting of pyrrolyl, pyrazolyl, imidazolyl, 1,2,3-triazolyl, 1,2,4-triazolyl, furanyl, oxazolyl, isoxazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, thiophenyl, thiazolyl, isothiazolyl, 1,2,3-thiadiazolyl, 1,3,4-thiadiazolyl, pyridyl, pyridazinyl, and
 5 benzimidazolyl, any of which may optionally be substituted with 1 to 3 substituents independently selected from the group consisting of halo, cyano, -SCF₃, (C₁-C₆)alkyl optionally further substituted with 1 to 6 fluoro substituents, and (C₁-C₆)alkoxy optionally further substituted with 1 to 6 fluoro substituents, and wherein pyridyl and pyridazinyl may also optionally be substituted with (C₁-C₆)alkylamino optionally
 10 further substituted with 1 to 6 fluoro substituents, (C₃-C₇)cycloalkyl(C₀-C₃)alkyl, or (C₃-C₇)cycloalkyl(C₀-C₃)alkyl-amino;

Het¹ is a saturated, nitrogen-containing heterocycle substituent selected from the group consisting of azetidyl, pyrrolidinyl, piperidinyl, homopiperidinyl, morpholinyl, thiomorpholinyl, homomorpholinyl, and homothiomorpholinyl, any of which may
 15 optionally be substituted with (C₁-C₆)alkyl or with 2 methyl substituents;

Het² is a saturated, oxygen-containing heterocycle substituent selected from the group consisting of tetrahydrofuranyl and tetrahydropyranyl, any of which may optionally be substituted with (C₁-C₆)alkyl or with 2 methyl substituents;

Ph¹ is phenyl optionally substituted with 1 to 5 independently selected halo substituents, or with 1 to 3 substituents independently selected from the group consisting of halo, cyano, -SCF₃, (C₁-C₆)alkyl optionally further substituted with 1 to 6 fluoro substituents, and (C₁-C₆)alkoxy optionally further substituted with 1 to 6 fluoro substituents;
 20

Ph² is phenyl substituted with:

- 25
- a) 1 to 5 independently selected halo substituents; or
 - b) 1 to 3 substituents independently selected from the group consisting of halo, cyano, -SCF₃, nitro, hydroxy, (C₁-C₆)alkyl optionally further substituted with 1 to 6 fluoro substituents, and (C₁-C₆)alkoxy optionally further substituted with 1 to 6 fluoro substituents; or

X-16115

-584-

c) 0, 1, or 2 substituents independently selected from the group consisting of halo, cyano, -SCF₃, methyl, -CF₃, methoxy, -OCF₃, nitro, and hydroxy, together with one substituent selected from the group consisting of

- 5
- i) (C₁-C₁₀)alkyl optionally further substituted with 1 to 6 fluoro substituents or mono-substituted with hydroxy, (C₁-C₆)alkoxy, (C₃-C₇)cycloalkyl(C₀-C₃)alkyloxy, Het²-(C₀-C₃)alkyloxy, Ph¹-(C₀-C₃)alkyloxy,
- 10
- ii) (C₁-C₁₀)alkoxy-(C₀-C₃)alkyl optionally further substituted with 1 to 6 fluoro substituents, and optionally further substituted with hydroxy,
- iii) (C₁-C₆)alkyl-C(O)-(C₀-C₅)alkyl optionally further substituted with 1 to 6 fluoro substituents,
- iv) carboxy,
- v) (C₁-C₆)alkoxycarbonyl optionally further substituted with 1 to 6 fluoro substituents,
- 15
- vi) (C₁-C₆)alkyl-C(O)-(C₀-C₃)-O- optionally further substituted with 1 to 6 fluoro substituents,
- vii) (C₁-C₆)alkylthio-(C₀-C₅)alkyl optionally further substituted with 1 to 6 fluoro substituents,
- viii) (C₁-C₆)alkylsulfinyl-(C₀-C₅)alkyl optionally further substituted with 1 to 6 fluoro substituents,
- 20
- ix) (C₁-C₆)alkylsulfonyl-(C₀-C₅)alkyl optionally further substituted with 1 to 6 fluoro substituents,
- x) (C₁-C₆)alkylsulfonyl-(C₀-C₃)alkyl-O- optionally further substituted with 1 to 6 fluoro substituents,
- 25
- xi) (C₃-C₇)cycloalkyl(C₀-C₃)alkyl, optionally further substituted on the cycloalkyl with 1 to 4 substituents selected from methyl and fluoro,
- xii) (C₃-C₇)cycloalkyl(C₀-C₃)alkyl-O-, optionally further substituted on the cycloalkyl with 1 to 4 substituents selected from methyl and fluoro,
- 30
- xiii) (C₃-C₇)cycloalkyl(C₀-C₃)alkyl-C(O)-,
- xiv) (C₃-C₇)cycloalkyl(C₀-C₃)alkyl-O-C(O)-,

X-16115

-585-

- xv) (C₃-C₇)cycloalkyl(C₀-C₃)alkyl-S-,
xvi) (C₃-C₇)cycloalkyl(C₀-C₃)alkyl-S(O)-,
xvii) (C₃-C₇)cycloalkyl(C₀-C₃)alkyl-S(O)₂-,
xviii) Ph¹-(C₀-C₃)alkyl, optionally substituted on the alkyl moiety with 1 to
5 2 fluoro substituents,
xix) Ph¹-(C₀-C₃)alkyl-O-, optionally substituted on the alkyl moiety with
1 to 2 fluoro substituents
xx) Ph¹-(C₀-C₃)alkyl-C(O)-,
xxi) Ph¹-(C₀-C₃)alkyl-O-C(O)-,
10 xxii) Ph¹-(C₀-C₃)alkyl-C(O)-(C₀-C₃)alkyl-O-,
xxiii) Ph¹-(C₀-C₃)alkylthio,
xxiv) Ph¹-(C₀-C₃)alkylsulfinyl,
xxv) Ph¹-(C₀-C₃)alkylsulfonyl,
xxvi) Ar²(C₀-C₃)alkyl,
15 xxvii) Ar²(C₀-C₃)alkyl-O-,
xxviii) Ar²(C₀-C₃)alkyl-S-,
xxix) Ar²(C₀-C₃)alkyl-C(O)-,
xxx) Ar²(C₀-C₃)alkyl-C(S)-,
xxxi) Ar²(C₀-C₃)alkylsulfinyl,
20 xxxii) Ar²(C₀-C₃)alkylsulfonyl,
xxxiii) Het¹(C₀-C₃)alkyl-C(O)- optionally substituted on the Het¹ moiety
with Ph¹,
xxxiv) Het¹(C₀-C₃)alkyl-C(S)- optionally substituted on the Het¹ moiety
with Ph¹,
25 xxxv) N-linked Het¹-C(O)-(C₀-C₃)alkyl-O-,
xxxvi) Het²-(C₀-C₃)alkyloxy,
xxxvii) R²⁶R²⁷N-,
xxxviii) R²⁸R²⁹-N-(C₁-C₃)alkoxy,
xxxix) R²⁸R²⁹N-C(O)-,
30 xl) R²⁸R²⁹N-C(O)-(C₁-C₃)alkyl-O-,
xli) R²⁸R²⁹N-C(S)-,

REPLACEMENT SHEET

AMENDED SHEET

2012-2005

X-16115

-586-

xlii) $R^{30}R^{31}N-S(O)_2-$,xlili) $HON=C(CH_3)-$, andxliv) $HON=C(Ph^1)-$,

or a pharmaceutically acceptable salt thereof, subject to the following provisos:

- 5 a) no more than two of R^1 , R^2 , R^3 , R^4 , and R^5 may be other than hydrogen;
b) when R^2 is methyl, then R^1 , R^3 , R^4 , and R^5 are each hydrogen; and
c) when R^3 is methyl, then R^2 and R^4 are each hydrogen.

10

2. A compound according to Claim 1 wherein R^7 is selected from halo, -CN,
15 and CF_3 .

3. A compound according to either Claim 1 or Claim 2 wherein R^7 is chloro.

4. A compound according to any one of Claims 1 to 3 wherein R^6 is $-C\equiv C-$
20 R^{10} .

5. A compound according to any one of Claims 1 to 3 wherein R^6 is $-O-R^{12}$.

6. A compound according to any one of Claims 1 to 3 wherein R^6 is $-S-R^{14}$.

25

7. A compound according to Claim 6 wherein R^6 is $-S-L-R^{15}$.

8. A compound according to Claim 7 wherein R^{15} is Ph^2 or Ar^2 .

9. A compound according to any one of Claims 1 to 3 wherein R^6 is -
30 $NR^{24}R^{25}$.

X-16115

-587-

10. A compound according to Claim 9 wherein R^{24} is $Ph^2-(C_1-C_3)$ *n*-alkyl-.
11. A compound according to Claim 9 wherein R^{24} is $Ar^2-(C_1-C_3)$ *n*-alkyl-.
- 5 12. A Compound according to any one of Claims 9 to 11 wherein R^{25} is hydrogen.
13. (Cancelled)
- 10 14. (Cancelled)
- 15 15. A compound according to any one of Claims 1 to 14 wherein R^1, R^2, R^3, R^4, R^5 , and R^8 , are each hydrogen.
16. A pharmaceutical composition comprising a compound according to any one of Claims 1 to 15 as an active ingredient in association with a pharmaceutically acceptable carrier, diluent or excipient.
- 20 17. A compound according to any one of Claims 1 to 15 for use in therapy.
18. A method for the treatment of obesity in mammals, comprising administering to a mammal in need of such treatment an effective amount of a compound according to Claim 1.
- 25 19. The method of Claim 18, where the mammal is human.

X-16115

-588-

20. A method for the treatment of obsessive compulsive disorder in mammals, comprising administering to a mammal in need of such treatment an effective amount of a compound according to Claim 1.

5 21. The method of Claim 20, where the mammal is human.

22. A method for the treatment of depression in mammals, comprising administering to a mammal in need of such treatment an effective amount of a compound according to Claim 1.

10

23. The method of Claim 22, where the mammal is human.

24. A method for the treatment of anxiety in mammals, comprising administering to a mammal in need of such treatment an effective amount of a compound according to Claim 1.

25. The method of Claim 24, where the mammal is human.

26. A compound according to any one of Claims 1 to 15 for use as a
20 pharmaceutical.

27. A compound according to any one of Claims 1 to 15 for use in the treatment of obesity in mammals.

25 28. A compound according to any one of Claims 1 to 15 for use in the
treatment of obsessive/compulsive disorder in mammals.

29. A compound according to any one of Claims 1 to 15 for use in the treatment of depression in mammals.

30

X-16115

-589-

30. A compound according to any one of Claims 1 to 15 for use in the treatment of anxiety in mammals.

5 31. A compound according to any one of Claims 27-30, where the mammal is a human.

10 32. The use of a compound according to any one of Claims 1 to 15 in the manufacture of a medicament for the treatment of a disorder selected from obesity, hyperphagia, obsessive/compulsive disorder, depression, anxiety, substance abuse, sleep disorder, hot flashes, and/or hypogonadism.

15 33. The use of a compound according to any one of Claims 1 to 15 in the manufacture of a medicament for the treatment of a disorder selected from obesity, obsessive/compulsive disorders, anxiety, or depression.

34. A pharmaceutical composition adapted for the treatment of obesity comprising a compound according to any one of Claims 1 to 15 in combination with one or more pharmaceutically acceptable excipients, carriers, or diluents therefore.

20 35. A pharmaceutical composition adapted for the treatment of obsessive/compulsive disorders comprising a compound according to any one of Claims 1 to 15 in combination with one or more pharmaceutically acceptable excipients, carriers, or diluents therefore.

25 36. A pharmaceutical composition adapted for the treatment of depression comprising a compound according to any one of Claims 1 to 15 in combination with one or more pharmaceutically acceptable excipients, carriers, or diluents therefore.

30 37. A pharmaceutical composition adapted for the treatment of anxiety comprising a compound according to any one of Claims 1 to 15 in combination with one or more pharmaceutically acceptable excipients, carriers, or diluents therefore.